REMARKS

Present Invention

The invention provides a method for producing a potato tuber lipoxygenase (LOX) with modified positional specificity toward arachidonic acid.

Pending Claims

Claims 12-28 are pending. Claims 24-28 are withdrawn.

Amendment to the Claims

Claim 12 has been amended to recite that the wild type potato tuber lipoxygenase comprises the amino acid sequence of SEQ ID NO: 3, which is the amino acid sequence set forth in Figure 3 and corresponds to EMBL database accession number S73865. This amendment is supported by the specification, for example, at page 4, lines 16-17, and Figure 3. Applicants note that, in the "Preliminary Amendment" dated January 8, 2002, the specification was amended to add the sequence identifier "SEQ ID NO: 3" to the description of Figure 3. However, a sequence listing containing the amino acid sequence set forth in Figure 3 was not filed with the Preliminary Amendment. A revised sequence listing (paper and computer readable copies) and certification are submitted concurrently herewith. Claim 12 also has been amended to recite a method of enhancing the specificity of a potato tuber lipoxygenase for position 11 of arachidonic acid comprising changing at least one amino acid in a wild type potato tuber lipoxygenase. This amendment is supported by the specification at, for example, page 2, lines 28-29. Claims 16 and 17 have been amended to replace the term "obtainable" with "obtained." Claims 22 and 23 have been amended to refer to an isolated cell. This amendment is supported by the specification at, for example, page 5, lines 20-21. Accordingly, no new matter has been added by way of these amendments.

Discussion of the Office Action

Claims 22-23 are rejected under 35 U.S.C. § 101 for allegedly encompassing non-statutory subject matter. Claims 12 and 13-23 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite. Claims 12-23 are rejected under 35 U.S.C. § 112, first paragraph, for an alleged lack of written description and nonenablement. Finally, claims 12-23 are rejected under 35 U.S.C. § 103, as allegedly unpatentable over the combined disclosures of Gan et al., *J. Biol. Chem.*, *271*: 25412-25418 (1996) ("the Gan reference"), Geerts et al., *Plant Physiol.*, *105*: 269-277 (1994) ("the Geerts reference"), and Sloane et al.,

Nature, 354: 149-152 (1991) ("the Sloane reference"). Reconsideration of these rejections is hereby requested.

Discussion of Rejection Under 35 U.S.C. § 101

Claims 22 and 23 are rejected under Section 101 because they allegedly encompass naturally occurring cells. Claims 22 and 23 have been amended to recite an "isolated" cell, thereby rendering the Section 101 rejection moot.

Discussion of Rejections Under 35 U.S.C. § 112, Second Paragraph

Claims 12-23 have been rejected under Section 112, second paragraph, as allegedly indefinite. In particular, the phrase "obtainable" in claims 16 and 17 allegedly renders those claims unclear. Claims 16 and 17 have been amended to replace the term "obtainable" with "obtained." Claim 12 is said to be indefinite because the recitation of an EMBL database accession number does not clearly define the lipoxygenase sequence. In addition, the phrase "corresponding to" in claim 12 allegedly is unclear. Claim 12 has been amended to refer to SEQ ID NO:3, which represents the amino acid sequence set forth in Figure 3 and disclosed in EMBL database accession number S73865, and to delete the phrase beginning with "corresponding to."

In view of the foregoing, claims 12-23 are definite, and the Section 112, second paragraph, rejections should be withdrawn.

Discussion of the Written Description and Enablement Rejections

Claims 12-23 have been rejected under 35 U.S.C. § 112, first paragraph, for an alleged lack of written description and nonenablement. Specifically, the Office Action alleges that the specification does not reasonably convey to the ordinarily skilled artisan that Applicants had possession of the claimed invention at the time the application was filed. The Office Action alleges that the claims are drawn to a genus of mutant lipoxygenase but, by teaching only one representative species (i.e., a potato tuber lipoxygenase), the application has not described the whole genus. With respect to enablement, the Office Action alleges that the specification is only enabling for the 5-lipoxygenase mutant from potato tuber disclosed in the application. Solely in an effort to advance prosecution of the subject application, and not in acquiescence of the rejection, claim 12 has been amended to recite a method of enhancing the specificity of a potato tuber lipoxygenase for position 11 of arachidonic acid comprising changing at least one amino acid in a wild type potato tuber lipoxygenase, which comprises the amino acid sequence of SEQ ID NO: 3. Accordingly, the

written description and enablement rejections under Section 112, first paragraph, are rendered moot by these amendments and should be withdrawn.

Discussion of Obviousness Rejection

Claims 12-23 have been rejected under Section 103 as allegedly obvious in view of the combined disclosures of the Gan reference, the Geerts reference, and the Sloane reference. This rejection is traversed for the reasons set forth below.

To establish a *prima facie* case of obviousness under Section 103 based on a combination of references, (i) the references must disclose or suggest every element of the claimed invention, (ii) there must be a motivation to combine the references, and (iii) the combination of references must provide a reasonable expectation of success for making the claimed invention. M.P.E.P. § 2143.

The Gan reference describes the structure of the arachidonic binding site of human 15-lipoxygenase. In particular, the Gan reference discloses that amino acid residues at positions 417 and 418 of human platelet 12 lipoxygenase and human reticulocyte 15 lipoxygenase correspond to amino acid residues at positions 556 and 557, respectively, of soybean lipoxygenase-1 (see page 25412, right column). These residues are said to be important features of the binding site for the methyl end of the fatty acid substrate. In addition, based on a sequence alignment that was not provided with the Office Action, these residues are said to correspond to an amino acid residue at position 576 of a potato tuber 5-lipoxygenase.

The Sloane reference reportedly discloses the identification of the amino acids that confer substrate specificity to human 12- and 15-lipoxygenases. In particular, the Sloane reference discloses that substitution of the amino acids at position 416, 417, and 418 affects the substrate specificity of each enzyme. The Geerts reference allegedly discloses a cDNA sequence encoding a potato tuber 5-lipoxygenase, as well as a vector and a host cell comprising the cDNA sequence.

In order to alter the enzyme's positional specificity for arachidonic acid, the Office Action contends that it would have been obvious to one of ordinary skill in the art at the time of the claimed invention to mutagenize the potato tuber lipoxygenase disclosed in the Geerts reference at amino acid position 576, and that one of ordinary skill in the art could have done so with a reasonable expectation of success. Applicants respectfully disagree. In this regard, the amino acid residues at positions 417 and 418 of human platelet 12-lipoxygenase and human reticulocyte 15-lipoxygenase disclosed in the Gan reference are said to be important features of the binding site for the methyl end of the fatty acid substrate. Applicants note, however, that the methyl end of the fatty substrate is not in the vicinity of the 5 position or

the 11 position of arachidonic acid. Thus, one of ordinary skill in the art would not expect that modifying the amino acids of a potato tuber lipoxygenase that correspond to positions 417 and 418 of a human lipoxygenase would enhance the specificity of the potato tuber lipoxygenase for position 11 of arachidonic acid.

Even if a *prima facie* case of obviousness were set out in the Office Action, the basis for the rejection is rebutted, and the obviousness rejection is overcome, by objective evidence of nonobviousness, which must be considered when determining obviousness (see, e.g., M.P.E.P. § 716.01(a)). Such evidence exists here. In particular, the Rule 132 Declaration of Dr. Ivo Feussner, submitted herewith, demonstrates that the method defined by claims 12-23 involves a mechanism that shifts potato tuber lipoxygenase specificity from the 5 position to the 11-position of arachidonic acid that is surprisingly different from the mechanism disclosed in the Sloane reference.

Finally, in making the obviousness rejection, the Office Action appears to contradict itself with respect to comments made in making the enablement rejection. Specifically, the Office Action alleges that one of ordinary skill in the art would not be able to identify amino acid residues in other plant lipoxygenases that correspond to amino acid 576 of a potato tuber lipoxygenase. Yet, in the obviousness rejection, the Office Action contends that one of ordinary skill in the art would be able to determine which amino acid residues of a human lipoxygenase and a soybean lipoxygenase correspond to the amino acid at position 576 of a potato tuber lipoxygenase.

For the foregoing reasons, the pending claims do not recite subject matter that is obvious in view of the Gan reference, the Sloane reference, and the Geerts reference. As such, the Section 103 rejection should be withdrawn.

Conclusion

The application is considered in good and proper form for allowance, and the Examiner is respectfully requested to pass this application to issue. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned agent.

Respectfully submitted,

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